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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/699,195	10/31/2003	Linda M. Pacioretty	CLANACCR_001NP	4532

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EXAMINER	
CHONG, YONG SOO	

ART UNIT	PAPER NUMBER
1627	

MAIL DATE	DELIVERY MODE
11/15/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/699,195	PACIORETTY ET AL.	
	Examiner	Art Unit	
	Yong S. Chong	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 March 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *1-20,25-27,30,31 and 36-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-24, 28-29, 32-35, 39-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/8/10 has been entered.

Claim(s) 1-40 are pending. Claim(s) 1-20, 25-27, 30-31, 36-38 have been withdrawn. Claim(s) 21 and 32 have been amended. Claim(s) 21-24, 28-29, 32-35, 39-40 are examined herein.

Applicant's arguments have been fully considered but found not persuasive. The rejection(s) of the last Office Action are maintained for reasons of record and modified below as a result of the new claim amendments.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim(s) 28-29, 39-40 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, claim(s) 28-29, 39-40 recites the

limitation "said thiol-containing compound" in claims 21 and 32. There is insufficient antecedent basis for this limitation in the claims.

Response to Arguments

Applicant agrees that there is insufficient antecedent bases and do not contest this rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham vs John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim(s) 21-24, 28-29, 32-35, 39-40 are rejected under 35 U.S.C. 103(a) as being obvious over McCleary (US Patent Application 2002/0132219 A1) and Medford et al. (US Patent 5,750,351) in view of Applicant's admission of the prior art.

The instant claims are directed to a method for treating or normalizing hyperlipidemia and/or subcutaneous fat loss and body wasting resulting from anti-retroviral treatment of HIV-1 infection in a subject by administering triglyceride of conjugated linoleic acid and N-acetylcysteine.

McCleary teach a nutritional supplement composition comprising conjugated linoleic acid and the antioxidant, coenzyme Q10, for modulating nutrient partitioning in a human (abstract). Hyperlipidemia is disclosed as a disorder due to nutrient partitioning (section 0002). More particularly, it is desirable to provide a means for modulating aberrant pathways of nutrient partitioning so as to avoid excessive fat storage, to promote oxidation of fat, and reduce fat levels (sections 0006 to 0007). McCleary also discloses specifically triglyceride of conjugated linoleic acid (section 0010). McCleary also teach that fat synthesis and storage are diminished resulting in a fall in the intracellular fat content of the liver, pancreas, and skeletal muscle as well as a fall in visceral fat and total body fat stores accompanied by a decrease in individual fat cell volume (section 0023). Preferred amounts for CLA are 50 mg to 20 g and for alpha-lipoic acid are 25 mg to 2 g (Table 1). Preferred amounts for coenzyme Q10 is about 5-500 mg (claim 6).

Medford et al. teach that activation of the transcriptional regulatory factor, NF-kB, is linked to hyperlipidemia. Importantly, activation of NF-kB can be inhibited by antioxidants such as N-acetylcysteine (col. 2, lines 6-14).

Generally, mere optimization of ranges will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such

concentration or temperature is critical. "When the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimal or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955); "The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages." *In re Peterson*, 315 F. 3d at 1330, 65 USPQ 2d at 1382; It has been held that it is within the skills in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. *In re Boesch*, 205 USPQ 215 (CCPA 1980) MPEP 2114.04

It would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to have substituted coenzyme Q10 in the composition as taught by McCleary with N-acetylcysteine as taught by Medford.

A person of ordinary skill in the art would have been motivated to make this substitution because: (1) of the functional equivalence of both coenzyme Q10 and N-acetylcysteine as well-known antioxidants; and (2) both McCleary and Medford are aimed at treating hyperlipidemia. Therefore, one of ordinary skill in the art would have had a reasonable expectation of success in treating hyperlipidemia with a composition comprising a conjugated linoleic acid and the antioxidant, N-acetylcysteine.

However, McCleary and Medford fail to specifically disclose a patient population with hyperlipidemia coincident with subcutaneous fat loss and body wasting resulting from anti-retroviral treatment from an HIV-1 infection.

Applicant's disclosure of the prior art teaches that HIV infection is accompanied by disturbances in lipid and glucose metabolism. These metabolic abnormalities are further confounded by hypercholesterolemia and hypertriglyceridemia (both subgenus to hyperlipidemia) induced by anti-retroviral drugs. In fact, it is estimated that almost two-thirds of HIV/AIDS patients exhibit abnormal fat distribution coincident with AR-therapy. Clinicians have termed this abnormal fat distribution lipodystrophy or fat maldistribution, which describe the syndrome of body shape changes related to changes in fat distribution in people with HIV/AIDS receiving AR-therapy (section 0003 to 0009).

It is noted that the above paragraph describes the specific patient population that is claimed since abnormal fat maldistribution is defined as subcutaneous fat loss and body wasting resulting from anti-retroviral treatment from an HIV-1 infection.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to have administered a composition comprising a conjugated linoleic acid and the antioxidant, N-acetylcysteine, as taught by McCleary and Medford to a patient with hyperlipidemia coincident with subcutaneous fat loss and body wasting resulting from anti-retroviral treatment from an HIV-1 infection.

A person of ordinary skill in the art would have been motivated to administer a composition comprising a conjugated linoleic acid and the antioxidant, N-acetylcysteine, as taught by McCleary and Medford to a patient with hyperlipidemia coincident with subcutaneous fat loss and body wasting resulting from anti-retroviral treatment from an HIV-1 infection because: (1) Applicant's admission of the prior art teaches that HIV infection is accompanied by disturbances in lipid and glucose metabolism and that

these metabolic abnormalities are further confounded by hypercholesterolemia and hypertriglyceridemia (both subgenus to hyperlipidemia) induced by anti-retroviral drugs; and (2) Applicant's admission of the prior art teaches that it is estimated that almost two-thirds of HIV/AIDS patients exhibit abnormal fat maldistribution, which describe the syndrome of body shape changes related to changes in fat distribution in people with HIV/AIDS receiving AR-therapy. Therefore, one of ordinary skill in the art would have had a reasonable expectation of success in treating a patient with hyperlipidemia coincident with subcutaneous fat loss and body wasting resulting from anti-retroviral treatment from an HIV-1 infection by administering a composition comprising a conjugated linoleic acid and N-acetylcysteine.

Response to Arguments

Applicant argues against the functional equivalence of between coenzyme Q10 and N-acetylcysteine as well known antioxidants. This assertion is based on CoQ10 being lipid soluble and NAC being water-soluble and the fact that both are structurally different.

This is not persuasive because these assertions raised by the Applicant do not affect the functional properties of the antioxidants. The differences in solubility affect the bioavailability and not the antioxidant properties. Furthermore, the instant claims do not recite any administration conditions that would prefer the composition to be water-soluble or lipid-soluble. With regards to the structure, the position taken by the

Examiner was not that coenzyme Q10 and N-acetylcysteine possesses the same structure, but that both are well known antioxidants.

Applicant argues that NF-kB is not linked to hyperlipidemia. Applicant goes on to explain a detailed mechanism of action involving VCAM-1 and LDL that somehow suggests that NF-kB is not linked to hyperlipidemia.

This is not persuasive because this argument does not rebut the general teaching that the transciptional factor, Nf-kB, integrates into a common molecular pathway involving hyperlipidemia. Medford mentions that the precise biochemical signals that activate NF-kB are not yet known, however this link is evident. Applicant's view of the mechanism of action goes against the teaching of Medford, therefore considered an invalid interpretation of the reference. Applicant is reminded that the standard for obviousness is not absolute but a reasonable expectation of success.

Applicant argues that CLA is not known to treat hyperlipidemia. While McCleary teaches a combination comprising CLA for the treatment of hyperlipidemia, at the time of the claimed invention seven of eight published clinical studies indicated a lack of effect of CLA on lowering blood lipids.

This is not persuasive because these clinical studies appear not to be conclusive because no long term studies were investigated. In fact, one of the seven appears to support the teachings of the McCleary reference. Nonetheless, Examiner does not view the eight published clinical studies as the state of the art regarding CLA's effect on blood lipids since it is in direct contradiction to the teachings of the McCleary reference.

The Babish Declaration #3 under 37 CFR 1.132 filed 3/8/10 is insufficient to overcome the rejection of claims 21-24, 28-29, 32-35, 39-40 based upon McCleary (US Patent Application 2002/0132219 A1) and Medford et al. (US Patent 5,750,351) in view of Applicant's admission of the prior art.

The Declaration seems make the case that CoQ10 and NAC are not functionally equivalent as antioxidants. The Declaration provides data in Exhibits B and C that show antioxidant activity for NAC, but no activity for CoQ10 when using various cell lines including the ones in Medford.

This is not persuasive because Applicant is reminded that both CoQ10 and NAC are well known antioxidants. Applicant cannot argue that that one does not possess antioxidant properties, otherwise why are they called "antioxidants" in the cited prior art? Moreover, the data reflected in Exhibits B and C are limited to the very small amounts used in the study and the specific cell lines. A much broader study involving a wide range of amounts for both CoQ10 and NAC would be more convincing. Therefore, a definitive conclusion cannot be said that that the antioxidant, CoQ10, does not have antioxidant properties.

In view of the foregoing, when all of the evidence is considered, the totality of the rebuttal evidence of nonobviousness fails to outweigh the evidence of obviousness.

Regarding the establishment of unexpected results, a few notable principles are well settled. It is applicant's burden to explain any proffered data and establish how any results therein should be taken to be unexpected and significant. See MPEP 716.02 (b). The claims must be commensurate in scope with any evidence of unexpected

results. See MPEP 716.02 (d). Further, a DECLARATION UNDER 37 CFR 1.132 must compare the claimed subject matter with the closest prior art in order to be effective to rebut a prima facie case of obviousness. See MPEP 716.02 (e). Applicants fail to provide clear and convincing evidence to support the alleged unexpected benefit.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong S. Chong whose telephone number is (571)-272-8513. The examiner can normally be reached on M-F, 9-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SREENI PADMANABHAN can be reached on (571)-272-0629. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Yong S. Chong/
Primary Examiner, Art Unit 1627

YSC